

What is claimed is:

1. A method for promoting angiogenesis in a tissue of a subject in need thereof,  
comprising:  
administering to the subject, an HMG CoA reductase inhibitor in an amount effective  
5 to promote angiogenesis in the tissue,  
wherein the subject is not otherwise in need of administration of an HMG CoA  
reductase inhibitor.
2. A method for treating a subject in need of increased blood flow to a tissue,  
10 comprising:  
administering to the tissue an HMG CoA reductase inhibitor in an amount effective to  
promote angiogenesis.
3. The method of claim 1, wherein the subject is nonhyperlipidemic and/or  
15 nonhypercholesterolemic.
4. The method of claim 1, wherein the subject has a condition selected from the group  
consisting of hypertension; diabetic peripheral vascular disease; gangrene; Buerger's  
syndrome; a wound; ischemia of the muscle, brain, kidney, lung, heart or limb; severe  
20 occlusive and/or obstructive vascular disease; peripheral vascular disease; myocardial  
ischemia; myocardial infarction; coronary artery disease; cerebral vascular disease; and  
visceral vascular disease.
5. The method of claim 1, further comprising the step of detecting angiogenesis in the  
25 tissue.
6. The method of claim 1, wherein the HMG CoA reductase inhibitor is a statin  
molecule.
- 30 7. The method of claim 6, wherein the statin molecule is selected from the group  
consisting of Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin  
(Lescol), Atorvastatin (Lipitor), or Cerivastatin (Baycol).

8. The method of claim 1, wherein the HMG CoA reductase inhibitor is administered orally.

5 9. The method of claim 1, wherein the HMG CoA reductase inhibitor is administered locally to a tissue requiring angiogenesis.

10. The method of claim 9, wherein the HMG CoA reductase inhibitor is a statin molecule.

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11. The method of claim 10, wherein the statin molecule is processed into the corresponding lactone form prior to local administration.

12. The method of claim 10, wherein the statin is selected from the group consisting of  
15 Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin (Lescol), Atorvastatin (Lipitor), or Cerivastatin (Baycol).

13. The method of claim 9, wherein administering comprises inserting a stent containing the HMG CoA reductase inhibitor into the tissue.

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14. The method of claim 9, wherein administering comprises administering to the subject a pharmaceutical composition comprises an HMG CoA reductase inhibitor and a pharmaceutically acceptable carrier.

25 15. The method of claim 14, wherein the pharmaceutical composition is formulated as a salve, gel, film or patch.

16. The method of claim 14, wherein the pharmaceutical composition is suitable for topical application.

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17. The method of claim 14, wherein the pharmaceutical composition is a controlled release matrix.

18. The method of claim 17, wherein the pharmaceutical composition is formulated to release the HMG CoA reductase inhibitor substantially continuously for a period of at least one day.

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19. The method of claim 14, wherein the pharmaceutical composition further comprises an angiogenic growth factor protein.

20. The method of claim 19, wherein the angiogenic growth factor protein is selected from the group consisting of acidic and basic fibroblast growth factors, vascular endothelial growth factor, epidermal growth factor, transforming growth factor  $\alpha$  and  $\beta$ , platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor  $\alpha$ , hepatocyte growth factor and insulin like growth factor.

21. The method of claim 14, wherein the pharmaceutical composition further comprises a nucleic acid encoding for an angiogenic growth factor protein.

22. The method of claim 21, wherein the nucleic acid encodes for an angiogenic growth factor protein selected from the group consisting of acidic and basic fibroblast growth factors, vascular endothelial growth factor, epidermal growth factor, transforming growth factor  $\alpha$  and  $\beta$ , platelet-derived endothelial cell growth factor, platelet-derived growth factor, tumor necrosis factor  $\alpha$ , hepatocyte growth factor and insulin like growth factor.

23. The method of claim 14, wherein the pharmaceutical composition further comprises an Akt protein.

24. The method of claim 23, wherein the Akt protein is selected from the group consisting of Akt-1, Akt-2 and Akt-3.

25. The method of claim 23, wherein the Akt protein is constitutively active.

26. The method of claim 14, wherein the pharmaceutical composition further comprises a nucleic acid encoding for an Akt protein.

27. The method of claim 26, wherein the nucleic encodes for an Akt protein selected from the group consisting of Akt-1, Akt-2 and Akt-3.

28. The method of claim 19, wherein the pharmaceutical composition is administered by direct injection to a location requiring angiogenesis.

29. The method of claim 19, wherein the pharmaceutical composition is administered intraarterially by a balloon catheter to a location requiring angiogenesis.

30. A method for activating an Akt polypeptide, comprising:  
contacting a cell containing an Akt polypeptide with an HMG CoA reductase inhibitor under conditions wherein the HMG CoA reductase inhibitor activates the Akt polypeptide.

31. The method of claim 30, wherein the cell is contacted with an HMG CoA reductase inhibitor *in vivo*.

32. The method of claim 30, further comprising the step of detecting the activated Akt polypeptide.

33. The method of claim 32, wherein detecting the activated Akt polypeptide comprises detecting a downstream signaling event.

34. The method of claim 33, wherein the downstream signaling event is selected from the group consisting of phosphorylation of an Akt substrate molecule, a change in the rate of protein degradation, a change in the level of mRNA transcription, a change in the level of protein translation, reduction of apoptosis and induction of angiogenesis.

35. The method of claim 30, wherein detecting the activated Akt polypeptide comprises detecting Akt polypeptide phosphorylation.

36. The method of claim 35, wherein detecting the activated Akt polypeptide comprises detecting Akt polypeptide phosphorylation at Ser 473 and/or Thr 308.

5 37. The method of claim 30, wherein the Akt polypeptide is expressed by an endothelial cell.

38. The method of claim 30, wherein the Akt polypeptide is selected from the group consisting of Akt-1, Akt-2 and Akt-3.

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39. The method of claim 30, wherein the Akt polypeptide has SEQ ID NO:1.

40. The method of claim 30, wherein the HMG CoA reductase inhibitor is a statin molecule.

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41. The method of claim 40, wherein the statin molecule is selected from the group consisting of Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin (Lescol), Atorvastatin (Lipitor), or Cerivastatin (Baycol), provided that when the statin molecule is an inhibitor of HMG CoA, it is processed into the corresponding lactone form prior to local administration.

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42. A method for promoting angiogenesis, comprising:  
contacting a cell containing an Akt polypeptide with an HMG CoA reductase inhibitor under conditions wherein the HMG CoA reductase inhibitor activates the Akt polypeptide.

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43. The method of claim 42, wherein the cell is contacted with an HMG CoA reductase inhibitor *in vivo*.

44. The method of claim 42, wherein the Akt polypeptide is activated due to phosphorylation at Ser 473 and/or Thr 308.

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45. The method of claim 42, wherein the Akt polypeptide is expressed by an endothelial cell.

46. The method of claim 42, wherein the Akt polypeptide is selected from the group  
5 consisting of Akt-1, Akt-2 and Akt-3.

47. The method of claim 42, wherein the Akt polypeptide has SEQ ID NO:1.

48. The method of claim 42, wherein the HMG CoA reductase inhibitor is a statin  
10 molecule.

49. The method of claim 48, wherein the statin molecule is selected from the group consisting of Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin (Lescol), Atorvastatin (Lipitor), or Cerivastatin (Baycol), provided that when the statin  
15 molecule is an inhibitor of HMG CoA, it is processed into the corresponding lactone form prior to local administration.

50. A screening method to identify an Akt activating compound, comprising:  
contacting a cell containing an Akt polypeptide with a putative Akt activating  
20 compound under conditions wherein an Akt activating compound activates the Akt polypeptide; and  
determining the level of Akt polypeptide activation in the presence and absence of the putative Akt activating compound,  
wherein an increase in the level of Akt polypeptide activation in the presence of the  
25 putative Akt activating compound relative to the level of Akt polypeptide activation in the absence of the putative Akt activating compound indicates that the putative Akt activating compound is an Akt activating compound.

51. The method of claim 50, wherein the Akt activating compound is an HMG CoA  
30 reductase inhibitor.

52. The method of claim 50, wherein the Akt polypeptide is expressed by an endothelial cell.

53. A method for treating a wound, comprising:

5       contacting the wound with a sufficient amount of an HMG CoA reductase inhibitor under conditions wherein the HMG CoA reductase inhibitor enhances healing of the wound.

54. The method of claim 53, wherein contacting the wound comprises locally administering the HMG CoA reductase inhibitor to the wound.

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55. The method of claim 53, wherein administering comprises administering to the subject a pharmaceutical composition containing an HMG CoA reductase inhibitor and a pharmaceutically acceptable carrier.

15   56. The method of claim 55, wherein the pharmaceutical composition is formulated as a salve, gel, film or patch.

57. The method of claim 55, wherein the pharmaceutical composition is suitable for topical application.

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58. The method of claim 55, wherein the pharmaceutical composition is a controlled release matrix.

59. The method of claim 55, wherein the pharmaceutical composition is formulated to  
25   release the HMG CoA reductase inhibitor substantially continuously for a period of at least one day.

60. The method of claim 53, wherein the wound is a surgical wound.

30   61. The method of claim 53, wherein the HMG CoA reductase inhibitor is selected from the group of Lovastatin (Mevacor), Pravastatin (Pravachol), Simvastatin (Zocor), Fluvastatin (Lescol), Atorvastatin (Lipitor), or Cerivastatin (Baycol), provided that when the statin

molecule is an inhibitor of HMG CoA, it is processed into the corresponding lactone form prior to local administration.

62. The method of claim 53, further comprising the step of detecting angiogenesis in the  
5 treated wound.